REMARKS

Applicants respectfully request reconsideration of the present application.

CLAIMS STATUS

Claims 8, 11-13, 15, 16, 18-34, 38 and 39 are pending.

REJECTION UNDER 35 U.S.C. § 103(a)

Claims 8, 11-13, 15, 16, 18-34, 38 and 39 stand rejected as obvious over SmithKline Beecham Co. (WO 95/06410 or the '410 document) in view of Sekine *et al.* (WO 97/28794 as translated by US 6,054,484) and RxList Monographs (1999). Applicants traverse the rejection.

The '410 document discloses angiotensin II receptor antagonist, 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate, in claim 13 and topical administration of angiotensin II receptor antagonists on page 29, lines 14-32. However, as admitted by the PTO, the '410 document fails to teach a permeability regulator comprising (A) fatty acid ester, (B) polyol and (C) non-ionic surfactant, see Office Action, page 3. Furthermore, the '410 document does not provide any suggestion or motivation to use such a regulator for topical administration of angiotensin II receptor antagonists.

Sekine teaches compositions for transdermal delivery of diclofenac sodium. One of Sekine's compositions, composition # 23, includes isopropyl myristate, propylene glycol and coconut fatty acid diethanolamide treated by the PTO as a fatty ester, a polyol and a non-ionic surfactant respectively. However, Sekine neither teaches 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate, nor provides any suggestion or motivation to substitute diclofenac sodium with any other compound.

The PTO uses RxList as evidencing insolubility of 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-

yl]methyl]benzimidazole-7-carboxylate, which is also known as Candesartan cilexetil, in water. The PTO notes that Sekine teaches that "diclofenac sodium has 1.5% solubility in water" and concludes that "when formulating a compound that is poorly soluble in water, such as Candesartan cilexetil into a transdermal delivery system, one of ordinary skill in the art could look to Sekine et al. as a method of formulating a compound that has poor solubility in water into a transdermal delivery device...", see Office Action, page 4.

In response, Applicants submit that the PTO failed to establish a *prima facie* case of obviousness. As explained above, the '410 document does not provide any suggestion or motivation to use a permeability regulator comprising (A) fatty acid ester, (B) polyol and (C) non-ionic surfactant for topical administration of angiotensin II receptor antagonists and Sekine does not provide any suggestion or motivation to substitute diclofenac sodium with 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate in his transdermal composition.

Furthermore, contrary to the PTO's assertion on page 3, one of ordinary skill in the art would not look to Sekine for formulating a transdermal composition of a compound, which is practically insoluble in water, such as Candesartan cilexetil. In the response filed November 7, 2006, Applicants presented evidence demonstrating that diclofenac sodium has a water solubility of 2.61 mg/mL at 20°C, while Candesartan ciletix under the same conditions has a water solubility of less than 0.00005 mg/mL, which is more than 50,000 times less than the water solubility of diclofenac sodium. To further emphasize the difference in water solubilities between diclofenac sodium and Candesartan ciletix, Applicants submit with the present communication page 2, THE PHARMACOPOEIA OF JAPAN, 12 ed., 1992, which provides classification of solubilities for pharmaceutical compounds. Based on the classification in THE PHARMACOPOEIA OF JAPAN, diclofenac sodium qualifies as sparingly soluble compound, as according to Sekine diclofenac sodium has 1.5 % water solubility, i.e. the amount of water required for dissolving 1 g of diclofenac sodium is 66.7 mL. Quite differently from diclofenac sodium, Candesartan ciletix qualifies as practically insoluble in water. In sum, Applicants submit that one of ordinary skill in the art would not have a required motivation and a required reasonable expectation of success to substitute a

sparingly water soluble compound, diclofenac sodium taught in Sekine with a practically water insoluble compound, Candesartan ciletix.

In conclusion, as the PTO failed to establish a *prima facie* case of obviousness, Applicants request withdrawal of the rejection.

For the record, Applicants address the "normal optimization" assertion by the PTO on page 4 of the Office Action. In this regard, Applicants respectfully submit that obviousness cannot be based on the manner in which an invention is made or merely on the level of ordinary skill in the art.

CONCLUSION

Applicants believe that the present application is in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are

needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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